

Amendments to the Specification:

Please replace the paragraph beginning at page 15, line 23 and extending through page 16, line 5, with the following amended paragraph:

An ELISA analysis was performed to demonstrate that it is possible to use an antibody that detects an epitope in the cleavage region to differentiate between proMMPs and activated MMPs. ELISA analysis was performed on polyclonal antibodies produced against an 11 mer peptide, GVPDLGRFQTF, that spans the activation cleavage region of MMP-9. One microgram of the MMP protein was mixed with human plasma and absorbed to the wells of a 96-well microtiter plate. The initial volume was 50 μ L. After the wells were blocked with phosphate buffered saline (PBS) supplemented with 10% nonfat dry milk (blocking buffer), polyclonal antibodies in PBS were added at various dilutions and allowed to react with the antigen at room temperature for one hour. Following three washes in PBS, visualization was achieved via a goat anti rabbit secondary antibody that was conjugated with horseradish peroxidase. The secondary antibody was added at a 1:2000 dilution in blocking buffer and incubated at room temperature for one hour. After three washes in PBS, color development was achieved by adding a solution containing 50 mM sodium citrate, 50 mM citric acid, 1 mg/mL o-phenylenediamine, and 0.006% H₂O₂. After suitable color development, typically 5 to 10 minutes of incubation at room temperature, 50 μ L of 2 M sulfuric acid was added to stop the reaction and stabilize the product. Absorbance was measured at 490 nm using an automatic ELISA plate reader.

Please replace the paragraph beginning at page 16, line 6, with the following amended paragraph:

As shown in FIG. 7, the antibodies cross reacted with both ~~all three~~ MMP forms, but preferentially cross react with the proMMP form. On the graph, the proMMP-9 is represented by closed circles and activated MMP-9 by open circles. The MMP activation region shows a high degree of primary sequence conservation. It is therefore expected that antibodies produced against this region will detect the proMMP form of

most wound site MMPs. Although the observation that sequences downstream of the cleavage site show less conservation, it may mean that antibodies can be produced that are specific for individual MMPs.

Please replace the paragraph beginning at page 16, line 18, with the following amended paragraph:

This example demonstrates the specific detection of the proenzyme form of wound site proteinases by polyclonal antibodies. The polyclonal antibodies produced here broaden the detection capabilities of the test and can be used directly in a variety of immunological formats including ELISA. They can also be modified prior to use for fluorescent or other assays. Hence, the polyclonal antibodies can be used in almost any clinical setting. An 11 amino acid peptide (GV~~P~~DLGRFQTF) that spans the cleavage site of MMP-9 was synthesized using standard peptide chemistries. Since small peptides do not illicit an immune response in animals, it was necessary to conjugate the peptide to a carrier protein. The peptide was conjugated to BSA using 1-ethyl-3-[3-dimethylaminopropyl]-carbodiimide (EDC). This material was used to produce polyclonal antibodies (pAbs) in rabbits. The resulting antisera was purified using standard antibody purification techniques. The purified pAbs reacted preferentially with proMMP-9 demonstrating that they detect ~~inactivated~~ ~~activated~~ MMP-9. They can also detect activated MMP-9 and the amino terminal proenzyme region, but to a much lesser extent. The detection of the various MMP forms can take place in simulated chronic wound fluid.